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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ORWIG, KEVIN S	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/575,449	ROYERE ET AL.	
	Examiner	Art Unit	
	Kevin S. Orwig	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,29 and 31-54* is/are pending in the application.

4a) Of the above claim(s) *49-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *28, 29, and 31-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. The amendments filed on Oct. 19, 2009 have been entered.

Status of the Claims

Claims 28, 29, 31-54 are pending. Claim 28 has been amended; claims 1-27 and 30 are cancelled; claims 49-54 are withdrawn. Claims 28, 29, and 31-48 are now under consideration. This Office Action is in response to the request for continued examination filed on Nov. 13, 2009.

OBJECTIONS/REJECTIONS WITHDRAWN

The rejection of claims 28, 29, 31-33, and 36-48 under 35 U.S.C. 103(a) over JANSEN and WESTESEN is withdrawn upon further consideration.

OBJECTIONS/REJECTIONS MAINTAINED

The objection to claim 47 is maintained as discussed below.

Claim Objections (Maintained)

Claim 47 is objected to because of the following informalities: the word "the" in line three is awkward and should be deleted.

NEW GROUNDS OF OBJECTION/REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28, 29, 31-33, and 36-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over JANSEN (U.S. 2004/0071716; Filed Feb. 20, 2002) in view of WESTESEN (U.S. 6,207,178; Issued Mar. 27, 2001) and MONDAIN-MONVAL (WO 01/33223; Published May 10, 2001) as evidenced by U.S. 6,866,838.

Since the WO document to Mondain-Monval is in French, the '838 Patent, which is the result of the national stage entry of the international application, is relied upon as an English language equivalent. Column and line numbers refer to the '838 Patent.

1. Jansen discloses water-in-oil-in-water (w/o/w) emulsions comprising adjuvants or therapeutical (i.e. active) agents and stabilizing agents (abstract; par. [0044]). These emulsions contain a dispersed water-in-oil (w/o) phase (i.e. a lipid phase) in a continuous aqueous phase (example 3). Jansen teaches the use of emulsifiers (i.e. stabilizing agents), including PEG-30 dipolyhydroxystearate (i.e. Arlacel P135), which comprises two fatty acid chains and one polyethylene glycol (PEG) chain of 30 polyethylene glycol units (examples 1-6). The dispersed lipid phase droplets in these emulsions are from 1-5 μm (example 3), which is considered monodisperse according to the instant specification (pars. [0029] and [0039]). Jansen does not teach the use of lipids that are crystallizable as defined in the instant specification.

2. However, Westesen discloses suspensions of solid lipid particles, which are oil-in-water emulsions of dispersed lipid phase particles in a continuous water phase (abstract; examples 1-3). The lipid particles (i.e. the lipid phase) taught by Westesen form matrices that carry bioactive agents (col. 10, lines 20-67). The solid lipid particles are made of fats including di- and tri-glycerides of long chain fatty acids that are solid at room temperature (i.e. crystallizable lipids) (col. 5, lines 23-26; col. 9, lines 20-29). It is noted that the crystallizable lipids may be tripalmitate, a saturated C_{16} fatty acid derivative.

3. Moreover, Mondain-Monval discloses compositions comprising nanospheres (of up to 1 μm) for drug delivery (abstract; col. 3, lines 1-5; col. 4, lines 35-42; col. 5, lines 1-15). Mondain-Monval teaches that such particles advantageously have a narrow particle size distribution (i.e. are monodisperse or isodisperse) (col. 1, lines 56-58). Mondain-Monval teaches how to make monodispersed compositions (col. 5, line 66 to col. 6, line 9; Example 1). In light of these teachings, it would have been *prima facie* obvious for an artisan to specifically make monodispersed compositions and the artisan would have been aware of how to do so.

4. Jansen teaches that an improvement over the prior art is to provide emulsions that are stable (abstract; pars. [0010], [0030], and [0037]), have utility in parenteral administration (pars. [0030] and [0049]) and have utility as vaccines (abstract; pars. [0001], [0012], and [0040]). Westesen teaches that the compositions are extremely stable (col. 12, lines 18-19; claim 1) and that they are useful as delivery systems for a variety of administration routes including, *inter alia*, parenteral (e.g. intravenous), nasal,

and pulmonary administration as well as useful as vaccines (abstract; col. 1, line 60 to col. 2, line 12; col. 5, lines 27-32). It is clear that difficulties in obtaining stable, fluid emulsions for the administration routes discussed above were recognized in the art and addressed by both Jansen and Westesen. In light of these teachings, the skilled artisan would have been motivated to include crystallizable lipids in the composition taught by Jansen with the expectation of producing a stable emulsion for the delivery of lipophilic active agents in the oil phase, which would be useful for a variety of administration routes. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to substitute known crystallizable lipid components as taught by Westesen in the emulsions of Jansen to prepare a monodispersed drug delivery system with the expected result of solving the same problem, reading on instant claims 28, 30, 33, 36, and 37.

5. Instant claim 29 recites the composition of claim 28 in which an inner aqueous phase is dispersed in the dispersed lipid phase. In this situation, the composition is a water-in-oil-in-water (w/o/w) emulsion. Jansen teaches w/o/w emulsions in which an "inner" aqueous phase is dispersed in an oil phase comprising Miglyol 840, which is in turn dispersed in another aqueous phase (example 3), reading on instant claim 29.

6. Westesen teaches that the lipid phase of their compositions may be approximately 11% by weight relative to the total composition weight (see example 2, where 7.84 g lipid phase is dispersed in water to a total weight of 70 g), which is within the range of 0.01-30% by weight, reading on instant claim 31.

7. Jansen teaches the use of Arlacel P135 (i.e. the stabilizing agent) at 3% by weight, which is within the range of 0.001-30% by weight, reading on instant claim 32.

8. The aqueous phases of the emulsions taught by Jansen contain antigens and phosphate buffered saline (PBS) (i.e. a salt). Since PBS contains sodium chloride, it is considered a cryoprotective agent as defined in the instant specification (paragraph [0046]) (example 3), reading on instant claims 38 and 39.

9. Jansen teaches that the bioactive agents may be antigens (i.e. proteins) that are present in the inner water phase. Furthermore, the lipid particles taught by Westesen form matrices that carry bioactive agents (col. 10, lines 20-67). These bioactive agents may be pharmaceutical active principles (col. 10, lines 32-60; col. 14, line 58 to col. 15, line 27), such as, *inter alia*, antibiotics (i.e. antibacterial agents), beta blockers, and vitamins (col. 10, lines 32-60). Westesen also teaches that the bioactive agents may be angiotensin converting enzyme (ACE) inhibitors (col. 10, line 40). Since ACE is an exopeptidase, it is a protease. ACE inhibitors are thus protease inhibitors, reading on instant claims 44-48.

10. Westesen teaches that their compositions may comprise mixtures of bioactive agents (abstract; col. 15, lines 52-53). Thus, these compositions can contain at least two active principles, reading on instant claim 40.

11. In the case of the w/o/w emulsion taught by Jansen (example 3) the lipid phase (i.e. the dispersed w/o emulsion) contains a water soluble active principle (the antigen compounds), reading on instant claim 41.

12. Westesen teaches the use of both water soluble compounds (col. 10, lines 26-31) and sparingly water soluble compounds (col. 14, lines 54-62) as bioactive agents. Westesen also teaches that their compositions may comprise mixtures of bioactive agents as described above in paragraph 10. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to include both a water soluble active principle and a sparingly water soluble active principle in the lipid phase of the emulsions taught by Jansen as needed to produce a drug delivery system to treat multiple conditions or to deliver multiple drugs for the same condition, reading on instant claims 42 and 43.

Response to Arguments

Applicants' arguments have been fully considered but are not persuasive. Applicants argue that the instant claims (e.g. independent claim 28) requires particles having a size of 1-6 μm (response, p. 10).

Applicants' arguments with respect to this particle size are not persuasive given that the claims recite a particle size from 0.3-10 μm, not 1-6 μm. In response to applicants' argument that the references fail to show certain features of applicants' invention, it is noted that the features upon which applicant relies (i.e., a particle size from 1-6 μm) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

It is noted that not only the particles of Jansen, but also the particles of Westesen meet the limitation of particle size as instantly claimed. Nonetheless, Jansen teaches

particles having a size from 1-5 μm, and would read on this limitation even if it were recited in the claims.

Applicants argue that the cited references teach different routes to obtain a stable composition. Applicants argue that the disclosed compositions differ form one another (emulsions vs. suspensions), and further argue that the artisan would not expect that the modification would *necessarily* have lead to a stable composition (response, p. 11).

First, it is noted that the alleged different routes are not excluded by the instant claims, which use the open "comprising" language. Second, the "suspensions" of Westesen are made by an emulsification process (abstract; col. 1, lines 22-23, 30-31, and 40-44), and are not as distinct as applicant alleges. Third, in response to applicants' argument that the two compositions are "different", the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Fourth, Westesen teaches that SLPs possess an enhanced chemical and physical stability compared to conventional lipid emulsions owing to the lower degree of unsaturated fatty acids and other properties (col. 5, lines 57-67; col. 6, lines 10-20). Thus, the artisan would not only have been motivated to use such components in Jansen's compositions, but would also have had more than a reasonable expectation of success in doing so. Regarding

applicants' assertion that stability is not guaranteed, the MPEP states that, "The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)". Further, "Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976)". See MPEP § 2143.02. In this case, both references disclose stable compositions and seek to solve the same problem, namely preparing stable compositions for the delivery of fat-soluble active agents useful for, *inter alia*, parenteral delivery. An artisan would clearly have a reasonable expectation of success in making the suggested modification, particularly in light of Westesen's teachings of the *increased stability* of compositions using crystallizable lipids.

Applicants point to a Rule 1.132 declaration by one of the inventors to support their position (response, p. 12).

It is noted that the declaration is an opinion put forward by one of the inventors named on the instant application. The declaration asserts, as was previously argued, that adding a crystallizable lipid to Jansen would increase the viscosity of the compositions. As previously noted, teachings of the prior art *supports* the combination of crystallizable lipids in Jansen's emulsions. For instance, as indicated in the prior Office action, both Jansen and Westesen are concerned with stable emulsion compositions that have utility in parenteral (e.g. intravenous) administration and that

have utility in vaccines. See pars. [0001], [0012], [0030], [0040], and [0049] of Jansen, and abstract; col. 1, line 60 to col. 2, line 12; col. 5, lines 27-32 of Westesen. Given that Westesen's compositions, which contain solid lipid particles (i.e. crystallizable lipids), are intended *primarily* for the parenteral route (col. 5, lines 28-31), it cannot be said that the addition of these same lipids would necessarily increase the viscosity of Jansen's compositions to such an extent as to make them unsuitable for parenteral administration, nor can it be said that the artisan would expect an increase in viscosity to such an unfavorable extent. Nor does the declaration make such a statement. While, the viscosity of the composition may be increased to some extent by making the suggested modification, the evidence of record is still in favor of the suitability of the combination for parenteral use. Moreover, Jansen recognizes problems with viscosity and teaches that with the disclosed emulsifiers adjuvants based on w/o emulsions that are stable and have a low viscosity can be obtained (abstract; pars. [0003]-[0004], [0011], [0037], and [0045]). Thus, the skilled artisan would know how to modify the viscosity, through routine optimization of the components of the composition, such as the emulsifiers as taught by Jansen.

The declaration further states that "only application of shear...would have allowed to obtain monodisperse lipid particles." The declaration suggests that only a certain device can produce monodisperse compositions. It is noted that no limitations regarding shear or any device or other preparation conditions are recited in the instant claims. Thus, applicants' declaration raises possible scope of enablement issues. Moreover, monodispersed emulsions have been made in the art by other methods and

devices, for example, see U.S. 5,326,484 at col. 2, line 46 to col. 3, line 26; U.S. 5,364,632 at cols. 9 and 13, U.S. 6,669,963 at col. 4, U.S. 2004/0116541 at par. [0005], and Bibette, J. (1991) J. Coll. Interface Sci. 147; 474. Given the prior art, applicants' assertion simply cannot be true. Applicants' assertion that that Jansen does not use shear is also not true. Jansen teaches both low and high shear mixing procedures (pars. [0045], [0051], [0053], and [0061]). To suggest otherwise disregards Jansen's explicit teachings. In total, the opinion evidence presented is not persuasive and is insufficient to overcome the *prima facie* case of obviousness that has been established.

Claims 28, 34, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jansen, Westesen, and Mondain-Monval as evidenced by as applied to claims 28-33 and 36-48 above in further view of RABUSSIER (U.S. 3,258,326; Issued Jun. 28, 1966).

13. The composition of instant claim 28 is taught by Jansen and Westesen as applied above. Neither Jansen nor Westesen teaches the use of a thickener or alginic acid salts.

14. However, the use of alginates as components in emulsions is well-known. For instance, Rabussier discloses formulations comprising stable oil-in-water emulsions (col. 2, line 31) and hydrophilic colloids (col. 2, lines 25-28) for delivery of active agents (col. 2, lines 19-22). The hydrophilic colloids taught by Rabussier may be alginates that are added to the water (i.e. the aqueous phase) to maintain stability of the suspension (col. 1, lines 34-42; col. 3, lines 63-72; claim 7). Furthermore, Rabussier teaches that the alginate may be used in 0.2% by weight (example 4). Since alginates were known

in the art in the instantly claimed weight % range, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to include this known component as a stabilizer in the composition taught by of Jansen and Westesen to prepare a more stable drug delivery system, reading on instant claims 34 and 35.

Response to Arguments

Applicants' arguments have been addressed *supra*, and that discussion is incorporated herein. No further arguments were presented regarding Rabussier.

Claims 28, 29, 31-39, 41, 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over BIBETTE (WO 01/021297; Published Mar. 29, 2001) in view of WO 99/07463; Published Feb. 18, 1999 (hereinafter '463) and NAKAMURA (WO 02/074260; Published Sep. 26, 2002), as evidenced by U.S. 7,214,717, U.S. 6,627,603, and U.S. 2004/0137019.

Since the WO documents to Bibette and Nakamura are in languages other than English (i.e. French and Japanese), the '717 and '603 Patents (to Bibette) and the '019 pre-grant publication (to Nakamura), which are the result of the respective national stage entries of the international applications, are relied upon as English language equivalents. Column, line, and paragraph numbers refer to the '717 or '603 Patents or the '019 application publication as appropriate. It is further noted that the primary and one of the secondary references applied are the work of one of the instant inventors, yet neither was provided to the Office on any IDS.

15. Bibette discloses monodisperse stable double w/o/w emulsions and methods of their preparation (title; abstract), and teaches that the compositions are advantageous for pharmaceuticals and/or cosmetics because of the ability to control release kinetics of agents contained in the emulsions (col. 1, lines 9-21). Bibette teaches the double emulsions are composed of a monodisperse inverse emulsion dispersed in an aqueous external phase, the inverse emulsion itself being composed of droplets of an aqueous internal phase dispersed in an oily phase and defines "monodisperse" in substantially the same way as the instant application (col. 1, lines 62-67; col. 2, lines 20-25; col. 7, lines 9-13; col. 8, lines 45-48; Example 1). Bibette teaches that the inner aqueous phase (i.e. internal to the lipid phase) preferably comprises an active substance (abstract; col. 1, lines 16-18; col. 5, lines 25-26). Thus, the lipid phase overall comprises an active substance. Bibette teaches how to control the size of the lipid globules of the lipid phase emulsion (col. 1, lines 38-43; col. 7, lines 60-63) and states that the dispersed lipid globules have a size notably between 2-10 μm (col. 8, lines 45-48; Examples 1 and 4; Figs. 2-4). Bibette teaches that the nature of the oily phase is not determinant in the invention and that the nature of the oil components is not critical (col. 4, lines 42-43; col. 5, lines 8-9). Bibette does not explicitly teach the use of crystallizable lipids. Bibette only discloses the use of one class of surfactant for the oily phase, namely polyglycerol polyricinoleate. However, the use of the crystallizable lipids and other surfactant components would have been obvious to a skilled artisan.

16. For example, '463 (also to Bibette) discloses monodisperse multiple w/o/w emulsions containing at least one active principle and solubilized by a surfactant

(abstract). Bibette teaches fat soluble surfactants such as polyglycerol polyricinoleate and polyalkylene dipolyhydroxystearates (i.e. a stabilizer comprising two fatty acid chains and one polyethylene glycol chain (col. 5, lines 17-18). Thus, '463 teaches an overlapping set of surfactants to that of Bibette and establishes the functional equivalence of the surfactants taught by Bibette and those instantly claimed.

17. Moreover, Nakamura discloses stable w/o/w emulsions that can carry active agents such as cosmetics, vitamins, and drugs (abstract; pars. [0013]-[0016]). Nakamura teaches that the oil phase is not particularly limited and can contain a liquid or solid oil component or mixtures thereof (pars. [0019] and [0028]). Nakamura teaches solid fats or waxes, any of which meets the definition of a crystallizable lipid in the instant specification (pars. [0021]-[0022]). Nakamura teaches glyceryl triisopalmitate (i.e. tripalmitin), a saturated C_{16} fatty acid derivative. In line with the teachings of '463, Nakamura teaches that the internal aqueous phase and oil phase are emulsified with an emulsifier having an HLB value of not more than 7, since using emulsifiers with higher HLB values does not give stable emulsions (par. [0029]). Nakamura teaches that particularly preferred emulsifiers include polyethyleneglycol dipolyhydroxystearate (i.e. Arlacel P135, which comprises two fatty acid chains and one polyethylene glycol (PEG) chain of 30 polyethylene glycol units) (par. [0032]).

18. In light of these teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to utilize a solid (i.e. crystallizable) lipid in the w/o/w emulsions of Calderon. Based on Nakamura's teachings, doing so represents substitution of one known element for another to obtain predictable results.

It would also have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used an equivalent surfactant, such as those taught by '463, particularly since Nakamura teaches that this surfactant is preferable to prepare stable w/o/w emulsions. Claims 28, 29, 33, 36, 37, and 41 are rendered obvious by Bibette, '463, and Nakamura.

19. Bibette teaches that the lipid phase can be less than 20% by weight (see Example 1), given the proportion of aqueous phase present in the oily phase. Also, Nakamura exemplifies w/o/w emulsions having between 0.01-30% wt. of the lipid phase (e.g. Tables I-III, Examples 8 and 9). Bibette teaches that the quantity of surfactants depends on the nature of the surfactant as well as the other constituents present and can be determined by a person skilled in the art (col. 3, lines 59-63). Further, Nakamura teaches that the amount of the emulsifier having an HLB value of 7 or less is preferably 0.01-10% by weight (par. [0033]). Thus, selecting such amounts would be mere routine optimization for a skilled artisan. Claims 31 and 32 are rendered obvious by Bibette, '463, and Nakamura.

20. Bibette teaches the use of a polysaccharide thickening agent, in an amount of 1-10 % wt., and teaches that alginates are the preferred thickening agents (abstract; col. 3, lines 1-17). Claims 34 and 35 are rendered obvious by Bibette, '463, and Nakamura.

21. Bibette teaches that the aqueous continuous phase preferably comprises osmotic pressure balancing agents such as sorbitol, glycerol, or various salts (col. 4, lines 3-14) (i.e. cryoprotective agents as defined in the instant specification). Claims 38 and 39 are rendered obvious by Bibette, '463, and Nakamura.

22. The teachings of Bibette, '463, and Nakamura are presented *supra*. Regarding the recitations of certain active agents, applicants are advised that the mere recitation of a particular active agent, without more, will not result in patentably distinguishing the claimed invention from the prior art. Bibette teaches that any type of active substance generally used in one or more of the pharmaceutical, cosmetic, pest and disease control, or food fields can be used in the invention. Bibette teaches these agents can be, *inter alia*, vitamins (i.e. nutrients), vaccines, anti-inflammatory agents, and anti-cancer agents, and preservatives (col. 5; lines, 29-39). Claims 44-46 are rendered obvious by Bibette, '463, and Nakamura.

Claims 29, 40, 42, 43, 47, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bibette in view of '463 and Nakamura, as applied to claims 28, 29, 31-39, 41, 44-46 above, and further in view of LIN (U.S.) and KRAFFT (U.S. 5,980,936; Issued Nov. 9, 1999).

23. The teachings of Bibette, '463, and Nakamura are presented *supra*. While Bibette only teaches an active agent in the internal aqueous phase, the use of active agents in any phase of the emulsion is no more than an obvious variation.

24. For example, Lin discloses w/o/w multiple emulsions in which vitamins or drugs can be included in either the oil or aqueous phase (abstract; col. 2, lines 5-19). Additionally, Krafft discloses multiple emulsions that for the delivery of various drugs and therapeutic agents (abstract; col. 3, lines 35-36). It is an object of the invention to deliver both lipophilic and hydrophilic compounds in a controlled way (col. 3, lines 9-12). Krafft teaches that both lipophilic and hydrophilic agents are advantageously delivered,

preferably water soluble bioactive agents are delivered in combination with a lipophilic or hydrophobic agent (col. 6, lines 51-57). In light of these teachings, it would have been *prima facie* obvious for an artisan to include both a hydrophilic and a hydrophobic agent in the compositions of Bibette since the artisan would recognize the advantages and efficiency of simultaneous drug delivery. Moreover, Krafft teaches a set of bioactive agents overlapping that of Bibette, and the set taught by Krafft includes ACE inhibitors (i.e. protease inhibitors) (col. 13, lines 52-66). Claims 40, 42, 43, 47, and 48 are rendered obvious by Bibette, '463, Nakamura, Lin, and Krafft.

Conclusion

Claims 28, 29, and 31-48 are rejected. No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin S. Orwig whose telephone number is (571)270-5869. The examiner can normally be reached Monday-Friday 7:00 am-4:00 pm (with alternate Fridays off). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached Monday-Friday 8:00 am-5:00 pm at (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin S Orwig/

/David J Blanchard/
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